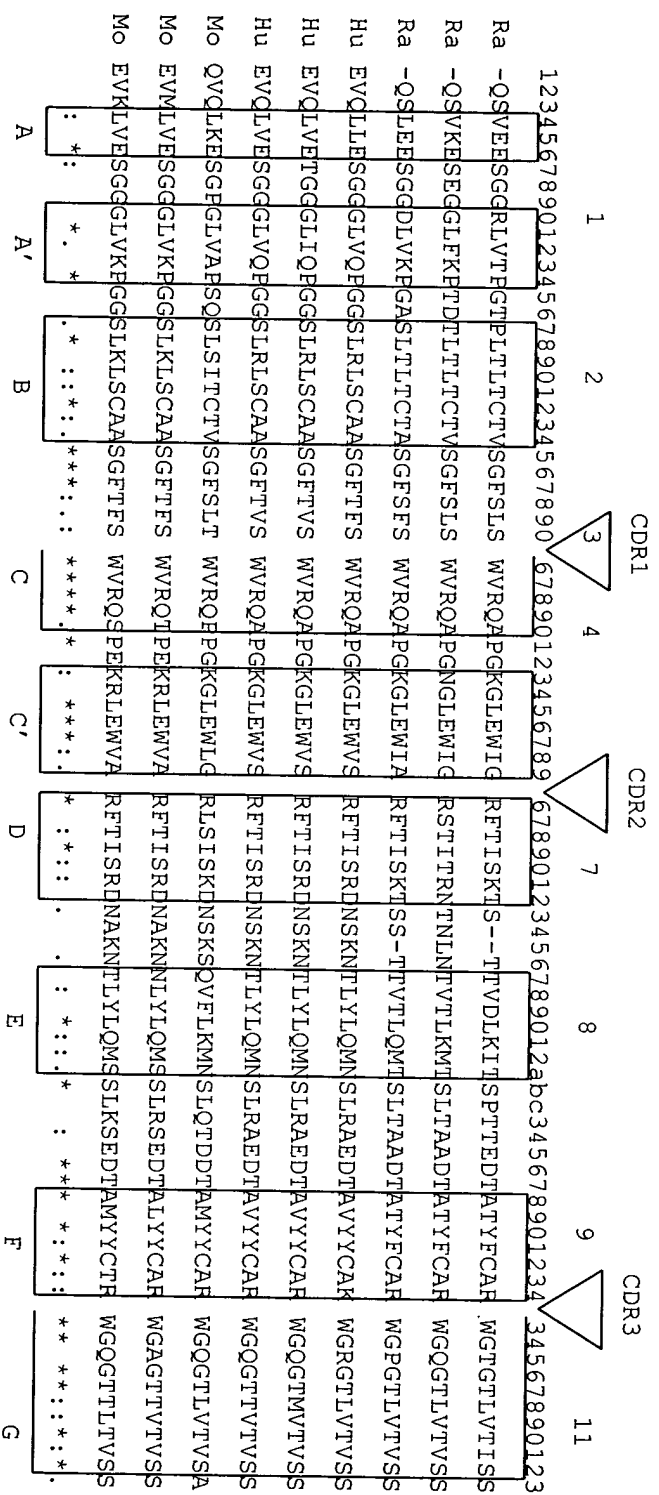


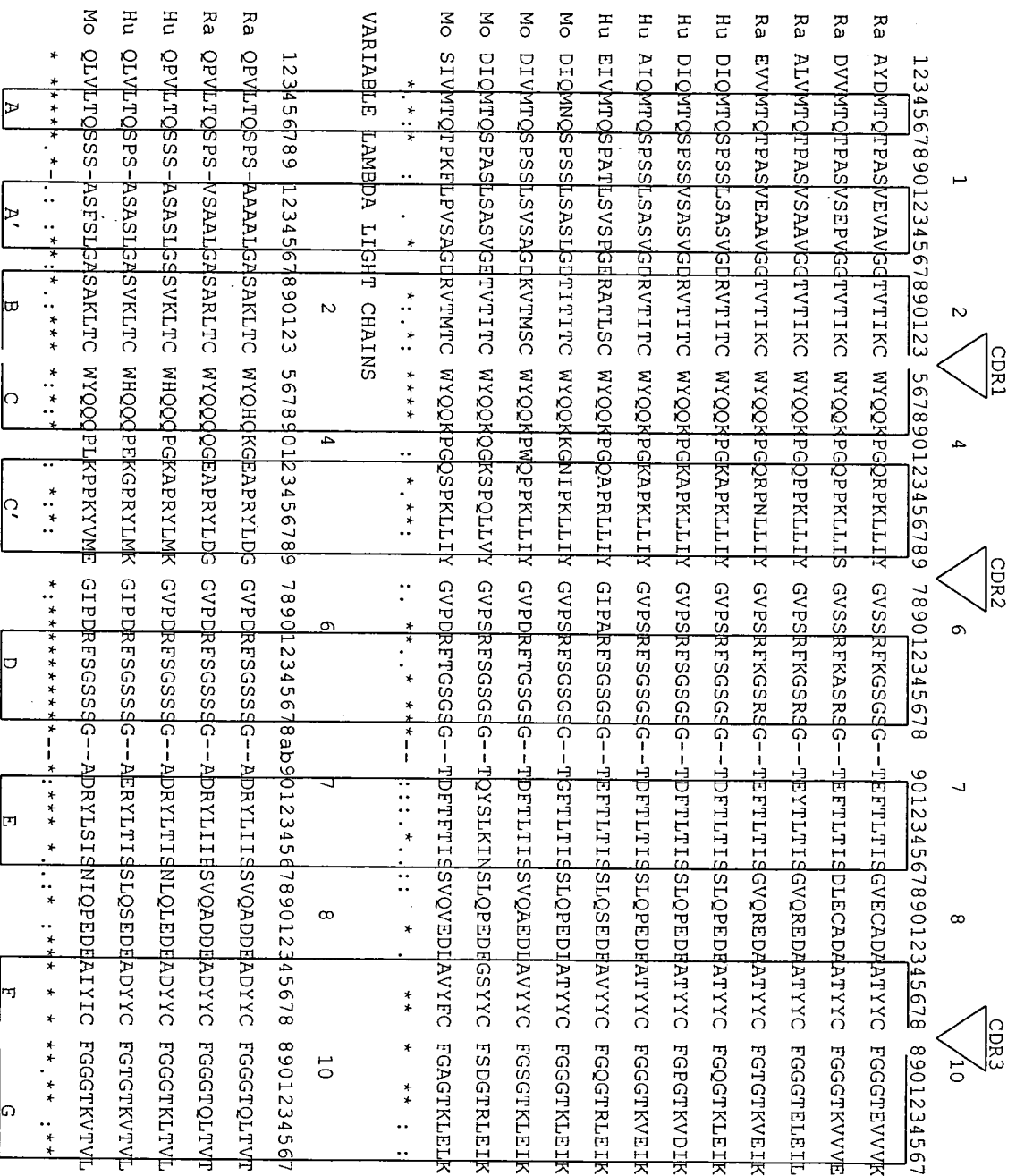
## VARIABLE HEAVY CHAINS



# Multiple sequence alignment of rabbit, human and murine VH frameworks

**FIG. 1A**

VARIABLE KAPPA LIGHT CHAINS



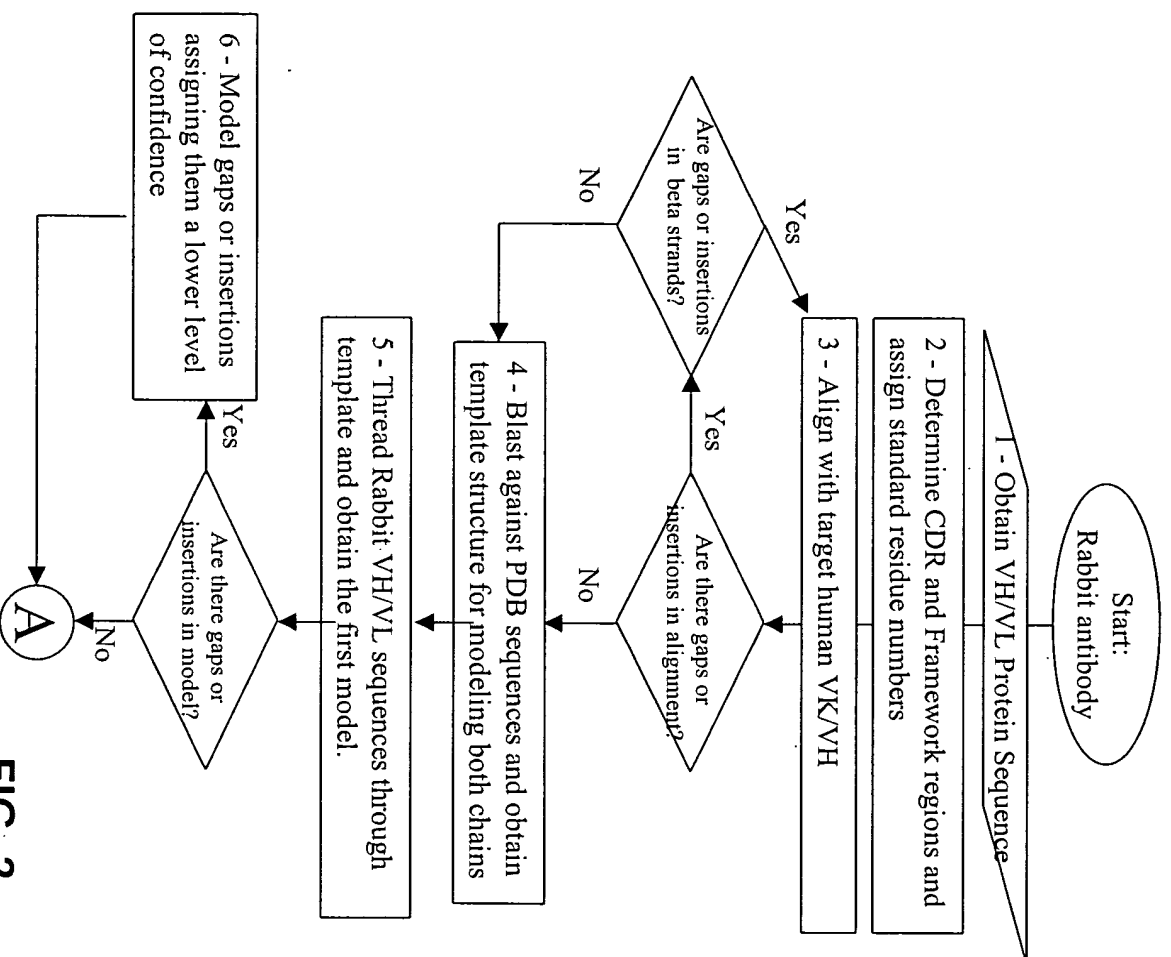
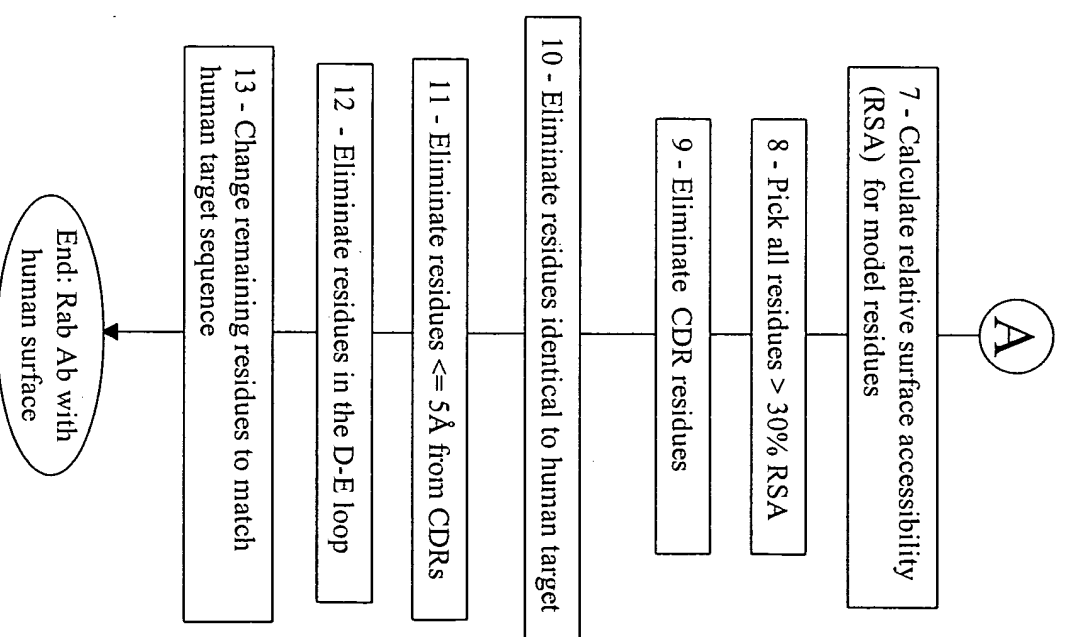


FIG. 2



FRAMEWORK 1 RELATIVE SOLVENT ACCESSIBILITY																							
VARIABLE KAPPA											V. LAMBDA			VARIABLE HEAVY									
	mouse 12E8	mouse 6FAB	mouse 2FBJ	mouse 1A2Y	rabbit B1mdl		human 2FB4	human 8FAB					mouse 12E8	mouse 6FAB	mouse 2FBJ	mouse B1mdl							
1	D	54	D	54	E	73	D	46	D	42	Q	60	.		1	E	73	E	52	E	77		
2	I	7	I	4	I	6	I	13	I	9	S	45			2	V	23	V	8	V	20	Q	31
3	V	32	Q	38	V	37	V	33	V	31	V	30	E	43	3	Q	30	Q	32	K	38	S	35
4	M	5	M	7	L	9	L	7	M	7	L	0	L	6	4	L	3	L	4	L	6	L	6
5	T	27	T	18	T	33	T	38	T	27	T	29	T	39	5	Q	35	Q	35	L	38	E	25
6	Q	4	Q	7	Q	8	Q	10	Q	8	Q	4	Q	8	6	Q	4	Q	4	E	7	E	0
7	S	38	I	34	S	23	S	27	T	35	P	21	P	18	7	S	14	S	27	S	27	S	17
8	Q	34	P	18	P	25	P	18	P	21	P	44	P	44	8	G	26	G	13	G	25	G	20
9	K	37	S	37	A	32	A	38	S	40	S	37	S	25	9	A	35	V	28	G	20	G	15
10	F	28	S	29	I	55	S	31	S	25													
11	M	17	L	17	T	13	L	14	V	13	A	6	V	15	10	E	24	E	24	G	13	G	25
12	S	26	S	32	A	22	S	37	S	26	S	30	S	19	11	V	33	L	36	L	29	L	47
13	T	1	A	5	A	0	A	1	A	12	G	2	V	4	12	V	7	V	7	V	7	V	9
14	S	16	S	23	S	17	S	17	A	28	T	26	S	20	13	R	46	R	45	Q	44	K	44
15	V	36	L	36	L	41	V	34	V	47	P	37	P	38	14	S	19	A	23	P	31	P	27
16	G	23	G	22	G	24	G	26	G	21	G	28	G	32	15	G	33	G	26	G	28	G	28
17	D	21	D	25	Q	26	E	26	G	12	Q	30	Q	36	16	A	11	S	18	G	10	A	15
18	R	27	R	48	K	46	T	34	T	41	R	52	T	26	17	S	35	S	21	S	35	S	26
19	V	2	V	3	V	6	V	7	V	12	V	4	A	1	18	V	7	V	3	L	9	L	14
20	S	21	S	27	T	31	T	28	T	29	T	28	R	46	19	K	36	K	33	K	42	A	29
21	I	1	I	0	I	2	I	3	I	2	I	1	I	1	20	L	0	M	0	L	0	L	0
22	T	29	S	20	T	23	T	21	K	37	S	28	T	25	21	S	13	S	12	S	17	T	24
23	C	3	C	0	C	0	C	0	C	1	C	1	C	0	22	C	1	C	0	C	0	C	0
															23	T	21	K	31	A	26	K	40
															24	A	6	A	5	A	6	A	1
															25	S	25	S	20	S	21	S	29
															26	G	39	G	33	G	30	G	37
															27	F	9	Y	13	F	10	F	13
															28	N	39	T	38	D	29	S	31
															29	I	1	F	5	F	0	F	3
															30	K	32	T	22	S	22	S	23

FIG. 3A

FRAMEWORK 2 RELATIVE SOLVENT ACCESSIBILITY																								
VARIABLE KAPPA										V. LAMBDA				VARIABLE HEAVY										
mouse 12E8		mouse 6FAB		mouse 2FBJ		mouse 1A2Y		rabbit B1mdl		human 2FB4		human 8FAB				mouse 12E8		mouse 6FAB		mouse 2FBJ		rabbit B1mdl		
35	W	0	W	0	W	0	W	1	1	W	1	W	0	36	W	0	W	1	W	0	W	3		
36	Y	0	Y	0	Y	0	Y	1	1	Y	0	Y	0	37	V	0	V	0	V	0	V	0		
37	Q	8	Q	5	Q	3	Q	12	Q	11	Q	13	Q	11	38	K	3	K	7	R	8	R	3	
38	Q	9	Q	6	Q	6	Q	8	Q	7	Q	1	Q	7	39	Q	16	Q	8	Q	8	Q	8	
39	K	22	K	25	K	26	K	29	K	21	L	31	K	16	40	R	16	R	30	A	10	A	19	
40	P	50	P	30	S	44	Q	61	P	51	P	36	P	47	41	P	35	P	36	P	42	P	49	
41	G	38	D	59	G	43	G	40	G	44	G	18	G	47	42	E	62	G	37	G	48	G	39	
42	Q	31	G	12	T	25	K	48	Q	41	M	34	R	38	43	K	39	Q	38	K	43	K	23	
43	S	12	T	35	S	7	S	9	P	20	A	23	A	15	44	G	13	G	17	G	13	G	16	
44	P	2	I	7	P	2	P	0	P	7	P	5	P	4	45	L	7	L	6	L	6	L	13	
45	K	32	K	33	K	34	Q	40	K	48	K	44	V	26	46	E	15	E	23	E	22	E	29	
46	L	4	L	2	P	13	L	13	L	9	L	8	M	5	47	W	5	W	2	W	3	W	5	
47	M	3	L	2	W	5	L	3	L	4	L	2	V	0	48	I	0	I	0	I	0	I	2	
48	I	0	I	0	I	0	V	0	I	0	I	0	I	0	49	G	0	G	0	G	0	A	0	
49	Y	16	Y	13	Y	20	Y	11	Y	27	Y	17	Y	11										

FIG. 3B

FRAMEWORK 3 RELATIVE SOLVENT ACCESSIBILITY																								
VARIABLE KAPPA										V. LAMBDA				VARIABLE HEAVY										
mouse 12E8		mouse 6FAB		mouse 2FBJ		mouse 1A2Y		rabbit B1mdl		human 2FB4		human 8FAB		mouse 12E8		mouse 6FAB		mouse 2FBJ		rabbit B1mdl				
57	G	40	G	35	G	38	G	44	G	38	G	43	G	41										
58	V	8	V	10	V	11	V	13	V	9	V	7	I	11										
59	P	21	P	21	P	14	P	24	P	24	P	22	P	19										
60	D	44	S	50	A	48	S	51	S	50	D	50	Q	58										
61	R	14	R	12	R	15	R	16	R	17	R	14	R	11	66	K	15	K	19	K	20	R	10	
62	F	1	F	1	F	2	F	3	F	2	F	4	F	3	67	A	4	T	2	F	0	F	3	
63	T	21	S	25	S	22	S	25	S	21	S	25	S	26	68	T	26	T	24	I	36	T	27	
64	G	6	G	6	G	8	G	6	G	4	G	12	S	7	69	M	4	L	1	I	1	I	5	
65	S	27	S	29	S	31	S	26	S	29	S	34	S	27	70	T	20	T	23	S	20	S	18	
66	G	20	G	15	G	15	G	21	G	22	K	27	T	32	71	A	20	V	15	R	7	K	16	
67	S	18	S	39	S	40	S	33	Y	48	S	40	S	37	72	D	26	D	21	D	29	T	35	
68	G	10	G	10	G	16	G	12	G	2	G	28	G	28	73	T	25	K	38	N	12			
															74	S	54	S	50	A	46	S	19	
															75	S	24	S	20	K	46	A	26	
69	T	19	T	18	T	24	T	24	T	15	A	14	T	22	76	N	9	S	15	N	17	T	32	
70	D	32	D	30	S	31	Q	37	E	34	S	25	T	13	77	T	4	T	3	S	4	T	19	
71	F	0	Y	1	Y	3	Y	2	F	0	A	2	V	1	78	A	1	A	2	L	0	V	4	
72	T	14	S	19	S	14	S	16	T	7	S	16	T	9	79	Y	22	Y	17	Y	13	T	19	
73	L	1	L	1	L	1	L	1	L	0	L	0	L	0	80	L	0	M	0	L	0	L	1	
74	T	4	T	10	T	9	K	28	T	14	A	4	T	12	81	Q	26	Q	27	Q	24	Q	22	
75	I	0	I	0	I	2	I	1	I	2	I	1	I	0	82	L	2	L	2	M	0	M	0	
76	S	18	S	30	N	31	N	22	S	17	G	24	S	28	82a	S	20	R	31	S	14	T	16	
77	N	34	N	25	T	23	S	30	D	38	G	6	G	19	82b	S	37	S	27	K	49	T	28	
78	M	0	L	2	M	0	L	0	L	11	L	2	V	1	82c	L	2	L	1	V	0	L	2	
79	Q	23	E	25	E	27	Q	27	E	24	Q	34	Q	23	83	T	24	T	18	R	42	T	21	
80	S	37	Q	26	A	10	P	39	C	42	S	36	A	38	84	S	32	S	38	S	32	A	34	
81	E	41	E	36	E	35	E	36	A	18	E	42	E	21	85	E	36	E	35	E	45	A	24	
82	D	0	D	0	D	2	D	1	D	1	D	1	D	2	86	D	3	D	4	D	2	D	0	
83	L	19	I	14	A	5	F	10	A	22	E	24	E	18	87	T	12	S	11	T	12	T	11	
84	A	3	A	2	A	2	G	8	A	2	T	6	A	0	88	A	1	A	2	A	1	A	1	
85	D	20	T	13	I	21	S	12	T	5	D	5	D	17	89	V	15	V	15	L	23	T	15	
86	Y	0	Y	0	Y	0	Y	0	Y	1	Y	0	Y	0	90	Y	1	Y	1	Y	0	Y	0	
87	F	2	F	1	Y	3	Y	4	Y	1	Y	3	Y	4	91	Y	5	F	1	Y	1	F	11	
88	C	0	C	0	C	0	C	0	C	0	C	0	C	0	92	C	0	C	0	C	0	C	0	
															93	N	1	A	0	A	0	A	0	
															94	A	0	R	6	R	4	R	17	

FIG. 3C

FRAMEWORK 4 RELATIVE SOLVENT ACCESSIBILITY																							
VARIABLE KAPPA										V. LAMBDA				VARIABLE HEAVY									
mouse 12E8		mouse 6FAB		mouse 2FBJ		mouse 1A2Y		rabbit B1mdl		human 2FB4		human 8FAB			mouse 12E8		mouse 6FAB		mouse 2FBJ		rabbit B1mdl		
98	F	7	F	7	F	9	F	8	F	5	F	4	F	8	103	W	3	W	10	W	11	W	9
99	G	1	G	1	G	3	G	2	G	2	G	1	G	2	104	G	0	G	5	G	1	G	1
100	A	27	G	30	A	47	G	36	G	26	T	30	G	33	105	Q	17	Q	36	Q	45	Q	32
101	G	8	G	4	G	6	G	7	G	13	G	6	G	7	106	G	6	G	11	G	14	G	10
102	T	1	T	0	T	0	T	1	T	0	T	0	T	0	107	T	0	T	1	T	8	V	8
103	K	24	K	27	K	26	K	32	E	16	K	33	K	18	108	L	29	T	29	L	12	L	35
104	L	2	L	2	L	1	L	3	V	15	V	0	L	0	109	V	0	L	1	V	0	V	0
105	E	8	E	5	E	12	E	25	V	21	T	19	T	4	110	T	11	T	13	T	8	T	20
106	L	19	I	5	L	4	I	49	V	46	V	4	V	6	111	V	4	V	12	V	5	V	2
107	K	29	K	27	K	35	K	45	K	45	L	30	L	16	112	S	10	S	10	S	12	S	23
															113	A	40	S	38	A	35	S	48

FIG. 3D

VII SEQUENCES  
Hu Human target sequence: Germline VH3-66 + JH4  
St Structure for homology modeling 1IGT chain A

## VK SEQUENCES

Hu Human target sequence: Germline VK L12 + JK4

B1	QASDNIYSLLA CDR1		YTSDLTS CDR2		QSYHYSKSTYVMV CDR3				
	1	2	4	6	7	8	10		
St	12345678901234567890123	567890123456789	7890123456789	789012345678	90123456789012345678		8901234		
Hu	DIVLVTQSPSSLSASLGDTITITC	WYQQKPGNIPKLLIY	GVPSRFSGSGSG-	TGFTLTITSSLQPEDIAITYYC			FGGGTKL		
B1	DIQMTQSPSTLSASVGRVTITC	WYQQKPGKAPKLLIY	GVPSRFSGSGSG-	TEFTLTITSSLQPEDFATYYC			FGGGTKV		
Ra	DIQMTQTPSSVSAAVGGTVTIKC	WYQQKPGQPPKLLIY	GVPSRFSGSGYV-	TEFTLTITSDLECAADAITYC			FGGGTEV		
Ra	AYDMTQTPASVEVAVGGTVTIKC	WYQQKPGQRPKLLIY	GVSSRFKSGSGSG-	TEFTLTITSGVECAADAITYC			FGGGTEV		
Ra	DVMTQTPASVSEPVGGTVTIKC	WYQQKPGQPPKLLIS	GVSSRFKASRSG-	TEFTLTITSDLECAADAITYC			FGGGTKV		
Ra	ALVMTQTPASVSAVGGTVTIKC	WYQQKPGQPPKLLIY	GVPSRFPKASRSG-	TEFTLTITSGVQREDAADAITYC			FGGGTEL		
Ra	EVVMTQTPASVEAAVGGTVTIKC	WYQQKPGQRPNNLIY	GVPSRFPKASRSG-	TEFTLTITSGVQREDAADAITYC			FGTGTKV		
Hu	DIQMTQSPSSLSASVGRVTITC	WYQQKPGKAPKLLIY	GVPSRFSGSGSG-	TDFTLTITSSLQPEDFATYYC			FGGGTKL		
Hu	DIQMTQSPSSVSASVGRVTITC	WYQQKPGKAPKLLIY	GVPSRFSGSGSG-	TDFTLTITSSLQPEDFATYYC			FGPGTKV		
Hu	AIQMTQSPSSLSASVGRVTITC	WYQQKPGKAPKLLIY	GVPSRFSGSGSG-	TDFTLTITSSLQPEDFATYYC			FGGGTKV		
Hu	EIVMTQSPATLSVSPGERATLSC	WYQQKPGQAPRLIY	GIPARFSGSGSG-	TEFTLTITSSLQSEDFAVYYC			FGGGTRL		
Mo	DIQMNQSPSSLSASLGDTITITC	WYQQKKGNIKLLIY	GVPSRFSGSGSG-	TGFTLTITSSLQPEDIAITYC			FGGGTKL		
Mo	DIQMTQSPSSLSASVAGDVVTMTC	WYQQKQWQPPKLLIY	GVPDRTFGSGSG-	TGFTLTITSSLQPEDLAVYYC			FGSGTKL		
Mo	DIQMTQSPASLSASVGTVTITC	WYQQKPGQSPQLLVY	GVPSRFSGSGSG-	TDYSLKINSLQPEDFASYYC			FGSDTRL		
Mo	SIIVMTQTPKFLPVSAGRVVTMTC	WYQQKPGQSPKLLIY	GVPDRFTGSGSG-	TDFTFTITSSVQEDLAVYYFC			FGAGTKL		
	A	A'	B	C	C'	D	E	F	G

**Fig. 4**